

**Conclusion:** The study findings support the field cancerisation concept. Genes that play a role in stromal-epithelial cell communication become more important with transition to cancer and represent potential molecular targets for early diagnosis and risk stratification.

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#### 0609: MOLECULAR REGULATION OF A NEWLY DISCOVERED STEM CELL MARKER PROTEIN, MOLECULAR REGULATION OF A NEWLY DISCOVERED STEM CELL MARKER PROTEIN. A STEP FORWARD TOWARDS CELL SELECTION FOR TISSUE ENGINEERING?

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**Aim:** Cartilage engineering using mesenchymal stem cells(MSCs) holds the potential to generate autologous cartilage tissues for surgical transplantation in the future. The perfect cocktail for MSC differentiation and cartilage production is still unknown. Previous laboratory data showed that orphan-receptor-tyrosine kinase(ROR2) positive MSCs demonstrated enhanced chondrogenesis and this was tested with the use of a ligand for ROR2, Wnt5a.

**Method:** MSCs were differentiated in monolayer and pellet cultures in the presence of Wnt5a with/or without TGF- $\beta$ 3. Gene and biochemical analyses were performed using rt-PCR and ELISA assays.

**Results:** In the presence of TGF- $\beta$ 3, Wnt5a induced a dose-dependent effect on the up-regulation of ECM synthesis and expression of cartilage-marker genes and in particular, type II collagen. These effects were shown to surpass those produced by the use of TGF- $\beta$ 3 only.

Wnt5a effectively promotes chondrogenesis only when used in combination with TGF- $\beta$ 3. ROR2 up-regulation appears essential to the chondrogenic action of Wnt5a. The results suggest a role of TGF- $\beta$ 3 in up-regulating the expression of ROR2 receptors to facilitate the interaction of Wnt5a with ROR2 in promoting chondrogenesis.

**Conclusion:** The discovery of the crucial interaction between TGF- $\beta$ 3, Wnt5a and ROR2 may have brought us one step closer to the utopia of high efficiency cartilage engineering.

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#### 0958: IN VITRO AND IN VIVO STUDY OF THE ROLE OF WDR11 IN IDIOPATHIC HYPOGONADOTROPIC HYPOGONADISM AND KALLMANN SYNDROME IN KNOCKOUT ANIMAL MODEL

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**Background:** In IHH/KS, the production of Gonadotropin-releasing-hormone(GnRH) is aberrant and reduced causing a failure of normal reproductive organ development and function. As a result, a knock-out(KO) mouse model(with disrupted WDR11 gene)has been genetically engineered to study the implications of WDR11 mutation on IHH/KS in these mice.

**Aims:** To genotype the newly generated KO mice that may potentially represent an animal model of IHH and KS. To validate the antibodies raised against WDR11 from commercial sources in order to confirm these genotypes at DNA and protein levels.

**Methods:** The genotypes of the KO mice offspring were determined using the polymerase chain reaction(PCR) method. Western blot method was used to validate the antibodies raised against WDR11.

**Results:** The genotypes of the pups from F1-F2 generations in the heterozygous and wild type pair were successfully identified and the Mendelian ratio was gratified. The heterozygous KO pups demonstrated syndactyly which is a phenotypic feature found in IHH/KS patients. The pups produced by the heterozygousKO pairs were smaller in size compared to heterozygousKO and wild type mice bred pups. Antibodies against WDR11 derived from the rabbit, goat and mouse were all validated.

**Conclusion:** WDR11gene disruption or mutation in these transgenic mice may cause similar reproductive disorder and other non-reproductive morphological changes as exhibited by IHH/KS patients.

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#### 1356: THE ROLE OF THE TRANSCRIPTION FACTOR NRF2 AS A POTENTIAL ENHANCER OF HEPATIC REGENERATION

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**Background:** The liver has a remarkable capacity for regeneration; however, acute hepatic failure remains a significant and often fatal complication following major hepatectomy. The transcription factor Nrf2 plays a pivotal role as a master regulator of cyto-protection, nevertheless, its role in hepatic regeneration is still ill-defined. We sought to investigate the prospect of Nrf2 as an enhancer of hepatic regeneration.

**Methods:** A murine model was used utilising C57BL/6J mice and two thirds partial hepatectomy was performed, followed by culling the mice at different time points. The liver tissue was collected at both the time of surgery and the time of cull. Pharmacological induction of Nrf2 was implemented by intra-peritoneal administration of CDDO-Me pre and post op. Nrf2 knockout mice were used as negative controls. Western blots for the proliferation marker PCNA were performed.

**Results:** A significant correlation between the increase of proliferation and Nrf2 activity was observed at 48 hours post-hepatectomy especially in the CDDO-Me treated mice as compared to the non-treated and knockout mice.

**Conclusions:** The transcription factor Nrf2 has a potential major role at the early stages of liver regeneration. Induction of Nrf2 peri-hepatectomy could decrease post-hepatectomy liver failure.

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#### 1370: DEVELOPMENT OF THE SURGICAL PROCEDURE FOR CELL TRANSPLANTATION IN AGE-RELATED MACULAR DEGENERATION

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**Background:** Age-related Macular Degeneration (AMD) is a leading cause of irreversible blindness. Retinal pigment epithelium (RPE) and Bruch's Membrane (BM) replacement have been stipulated as a possible treatment option. The aim of this study was to use vitrectomy techniques to implant aRPE19 cell graft into the subretinal space in ex-vivo porcine eyes.

**Method:** aRPE19 cells were cultured on a polyurethane (PU) membrane to form a stable, confluent monolayer. While a 3-port 23-gauge vitrector was used for subretinal transplantation of the graft with the aid of a chute device. A pilot dextran transport study was conducted on a number of membranes with and without cultured aRPE19 cells to identify a suitable BM prosthesis.

**Results:** Transplantation of the graft in the subretinal space was possible. The PU membrane could be visualised between the choroid and retina with aRPE-19 cells placed in the correct apicobasal orientation. No statistical difference was found in dextran transport studies between acellular and cellular membranes, and the treated expanded polytetrafluoroethylene (ePTFE) membranes were found to be the most porous.

**Conclusion:** aRPE19 cells could be successfully transplanted in the submacular region however alternative cell sources must be found. Treated ePTFE membranes may be a promising candidate for transplantation.

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### Surgical training & education prize

#### 0357: THE INFLUENCE OF COGNITIVE LOAD ON TECHNICAL ABILITY AMONG SURGICAL TRAINEES

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**Aims:** Intra-operative complications may place added cognitive strain on surgeons, requiring them to perform technical manoeuvres swiftly yet